REMARKS

I. OVERVIEW

Applicants have reviewed and considered the Office Action dated February 23, 2006. Claims 1-17 are pending in the instant application. Applicants have amended claims 3-5, 8, 9, 11-13, and 16. Support for these amendments and new claims 18-22 can be found in the Published Specification at paragraphs 7, 196, 198, and 208. Applicants would like to thank Examiner Saidha for his quick response to Applicants' telephonic inquiry regarding discrepancies with respect to the GenBank Accession Numbers cited in the § 112 rejection. Applicants found the information provided clarified the discrepancies. Applicants respectfully request reconsideration of the above-identified application in view of the amendments above and remarks that follow.

II. OBJECTIONS

A. The Examiner writes that the instant specification, page 1, line 6, the current status of U.S. Application Serial No. 09/896,301, filed June 29, 2001, must be updated, i.e., now abandoned.

Applicants thank Examiner for pointing out this discrepancy and accordingly have amended the Specification.

B. The Examiner writes that claims 8 and 12 are objected to under 37 C.F.R. § 1.75(c) as being of improper dependent form for failing to further limit the subject matter of a previous claim. The Examiner writes that the Applicant is required to cancel the claims, or amend the claims to place the claims in proper dependent form, or rewrite the claims in

independent form. The Examiner writes that 8 and 12 depend from non-elected claims 5 and 11 respectively.

Applicants disagree and respectfully submit that claims 8 and 12 as drafted are product-by-process claims. Although 37 CFR 1.75(c) requires the dependent claim to further limit a preceding claim, this rule does not apply to product-by-process claims as stated in MPEP § 601.08(n). Applicants request that these objections be withdrawn.

III. 35 U.S.C. § 112

A. Claims 8 and 12 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Examiner writes the work of Shcherban et al., PNAS (1995, September 26), 92 (20):9245-9, cited in the IDS, not prior art, have identified four distinct expansins cDNA in rice and at least six in *Arabidopsis* and show that the expansins from among these plant species are highly conserved in size and sequence similarity (60-87% amino acid sequence identity). The Examiner writes that Sequence homology of expansin from Strawberry (Patent No. 6,350,935, Seq Id No. 4), for example, and Applicants' amino acid sequence from *Arabidopsis* expansin (SEQ ID NO:5) show a sequence homology of about 48.9%; and a nucleotide sequence homology of 25% between Applicants' SEQ ID NO:1 (cucumber expansin cDNA, AC:AAT13320) and the nucleotide sequence of strawberry expansin (AC:AAV68447). The Office Action states that such a low nucleotide sequence homology is insufficient guidance and/or description to prepare or design specific probes or primers which may be 4-30 nucleotides in length using SEQ ID NOS:1 and 7 with no description of the

hybridization conditions to work with. The Office Action states that in the instant case, the specification fails to describe even a single cDNA fragment or a primer of SEQ ID NO:1 which is 4-30 nucleotides in length by structural and/or physical and chemical characteristics, representative of the entire genus.

Applicants disagree. Applicants respectfully submit that the use of the expansins identified by Shcherban after Applicants' filing date is improper. Applicants respectfully direct the Examiner's attention to MPEP § 2124 which states "it is impermissible to use a later factual reference to determine whether the application is enabled or described as required under 35 U.S.C. § 112, first paragraph." MPEP § 2124, citing *In re Koller*, 613 F.2d 819, 823 n. 5, 204 USPQ 702, 706 n.5 (CCPA 1980).

Applicants respectfully remind the Examiner that that "The Examiner has the initial burden, after a thorough reading and evaluation of the content of the application, of presenting evidence or reasons why a person skilled in the art would not recognize the written description of the invention provides support for the claims. There is a strong presumption that an adequate written description of the claimed invention is present in the specification as filed", citing *In re Wertheim*, 541 F.2d 257, 262, 191 USPQ 90, 96 (C.C.P.A. 1976). Guidelines for Examination of Patent Applications Under the 35 U.S.C. § 112, 1 ¶, Written Description requirement. Federal Register, Vol. 66, No. 4, January 5th, 2001.

Furthermore, the written description requirement is met if the patent specification describes the invention "in sufficient detail that one skilled in the art can clearly conclude that the inventor invented the claimed invention". *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1566, 43 U.S.P.Q.2d, 1398, 1404 (Fed. Cir.), rehearing, en banc, denied. In *Eli Lilly*, the Federal Circuit squarely dealt with the issue of written descriptions for claims

directed to genetic material. In order to satisfy the written description requirement the Court held that

> a description of a genus of cDNAs may be achieved by means of a recitation of a representative number of the cDNAs, defined by a nucleotide sequence, falling within the scope of a genus or of a recitation of structural features, common to members of the genus, which features constitute a substantial portion of the genus. Id. 1569.

The court emphasized that the written description must provide structural features common to the members of the genus which allows one of ordinary skill in the art to "visualize or recognize the identity of the members of the genus." (*Eli Lilly & Co.*, 118 F.3d at 1568). Thus, the standard to be used in determining whether or not the written description requirement has been satisfied is whether one of ordinary skill in the art can "visualize or recognize" the members of the genus based on the Applicant's disclosure. The specification teaches primers and probes of isolated nucleic acid molecules having the nucleotide sequence of SEQ ID NO:1 or obtained from SEQ ID NO:7. SEQ ID NOS:1 and 7 located in the sequence listing provide the complete nucleotide and amino acid sequences of an expansin, respectively. Applicants therefore submit that the written description fully sets forth the claimed invention so that one of ordinary skill in the art can reasonably "visualize or recognize" the members of the genus. Specifically, the structural features common to the members of a genus which would allow one of ordinary skill in the art to "visualize or recognize the identity of the members of the genus" are provided in SEQ ID NOS:1 and 7. This is because SEQ ID NOS:1 and 7 provided the critical sequences that allow one of ordinary skill in the art to identify the polynucleotides encompassed by the claims. Applicants are not claiming any or all polynucleotides encoding an expansin polypeptide. Rather, Applicants are claiming an isolated polynucleotide encoding a protein with expansin activity detected using specific hybridization conditions, a polynucleotide having at least 90% identity

with a polynucleotide of the sequence shown in SEQ ID NO: 1 or a polynucleotide identified using SEQ ID NO:1 or 7 with a specific biological function, expansin activity, as set forth in the Published Specification, at paragraphs 142-143. Thus, expansin polynucleotides or polypeptides are limited by the methods of claims 5 and 11. In view of the arguments above, Applicants assert that the claims and associated dependent claims are adequately supported by the Specification.

Applicants have amended claim 5 to recite "wherein a nucleotide sequence of said oligonucleotide is obtained by: aligning two or more nucleotide sequences of expansins according to sequence identity to identify a conserved sequence in said expansin sequences". Support for this amendment can be found in the Published Specification, at paragraph 196. As shown by Applicants, one skilled in the art can design primers for identifying a nucleotide sequence that encodes an expansin protein based on the amino acid sequence of an expansin protein. Published Specification, at paragraph 196. In addition, one skilled in the art can identify a novel nucleotide sequence encoding an expansin protein by aligning the amino acid sequences from various expansin proteins, using, for example, a Clustal W algorithm, and identify highly conserved regions among the proteins. Once such regions are identified, one skilled in the art can reverse translate the amino acid sequence found in these regions and design primers or probes in regions of low degeneracy. In addition, since the nucleotide sequence of Ex-29, a cucumber expansin identified by Applicants, is known, one can align the nucleotide sequence with other identified expansin cDNAs and prepare primers and probes to conserved regions from that information. Thus, it is possible to design primers that amplify other expansins and probes that detect other expansins based on knowledge from known nucleic acid or amino acid expansin sequences as successfully demonstrated by Applicants. Published Specification, at paragraph 196.

Thus the written description standard is fulfilled by both what is specifically disclosed and what is conventional or well known to one skilled in the art. SEQ ID NOS:1 and 7 are specifically disclosed in the application. The Specification describes in detail parameters for hybridization and preparation of probes as well as parameters for PCR amplification and primers in addition to the teaching in the claims. Published Specification, paragraphs 114-116, 195-196, and 98-108. In addition, the technology for determining hybridization probes and PCR amplification primers is well known in the art. As described above, one skilled in the art can determine conserved regions of expansin cDNAs and proteins and design primers or probes to those areas. Applicants further submit that given the polynucleotide sequence of SEQ ID NO:1 and polypeptide sequence of SEQ ID NO:7 it would be redundant to list those specific sequences for probes and primers. The structures of SEQ ID NO:1 and SEQ ID NO:7 provide the blueprint for all probes and primers thereof. Listing all possible probes and primers of SEQ ID NOS:1 and 7 is an unwarranted exercise which would needlessly encumber the specification. Accordingly, the specification provides an adequate written description of the probes and primers used in the claims. For the reasons argued above, Applicants respectfully request that the Examiner withdraw the written description rejection of the claims.

B. Claims 2-3, 8 and 12 stand rejected under 35 U.S.C. § 112, first paragraph, because the Examiner writes, the specification, while being enabling for a polynucleotide sequence encoding an expansin protein wherein the polynucleotide sequence hybridizes under high stringency conditions (6X, SSC, 50% formamide .....65°C for 15 minutes) to the sequence of SEQ ID NO:1 or a method for identifying a nucleic acid sequence which encodes a protein with expansin activity, comprising the steps of isolating the nucleic acid sequence from a cDNA

library by hybridization (under defined stringency conditions) using a DNA probe comprising the sequence of SEQ ID NO:1, does not reasonably provide enablement for a polynucleotide that is at least 90% identical to the sequence of SEQ ID NO:1 (claim 2) or a polynucleotide that encodes a polypeptide having at least 90% sequence identity to the sequences of SEQ ID NOS:2-7 (claim 3); or the method of identifying a nucleic acid comprising an oligonucleotide probe of 4-30 contiguous bases of SEQ ID NO:1 (claim 8), or by using an undefined primer of claim 12. The Examiner writes that with regard to the method claims 8 and 12 (dependent upon non-elected claims 5 and 11 respectively) nucleic acid hybridization or amplification assays are extremely sensitive to the conditions in which they are performed. The Examiner writes therefore, without a clear and explicit recitation of the conditions which were actually used by Applicants in isolating the claimed polynucleotides which hybridize to the disclosed sequences, the skilled artisan would not be able to practice the claimed invention and would not be reasonably apprised of the metes and bounds of the claimed invention. The Examiner writes that without such guidance, the experimentation left to those skilled in the art is undue.

Applicants respectfully disagree. The Examiner shows that several expansins identified after Applicants filing date have varying levels of sequence similarity to Applicants'. Applicants respectfully submit that the use of the expansins identified by Shcherban after Applicants' filing date to support the contention that Applicants specification is not enabled is improper. Applicants respectfully direct the Examiner's attention to MPEP § 2124 which states "it is impermissible to use a later factual reference to determine whether the application is enabled or described as required under 35 U.S.C. § 112, first paragraph." MPEP § 2124, citing *In re Koller*, 613 F.2d 819, 823 n. 5, 204 USPQ 702, 706 n.5 (CCPA 1980).

Even if the use of Shcherban reference was proper, the Examiner has not shown that the sequences with sequence similarity to Applicants do not behave as expansins. Applicants have provided ample guidance for the methods claimed to allow one skilled in the art to make and use the invention described in the claims without undue experimentation. Applicants submit that the Examiner has ignored the Specification's teachings and failed to make a *prima facie* case of non-enablement. It should be noted that "A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. § 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support." MPEP § 2164.04.

Furthermore, "it is incumbent upon the Patent Office ... to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement." MPEP § 2164.04. The rejection fails to satisfy this standard as it has provided no substantial reason to doubt the objective truth of the statements made by Applicants in its Specification as to the scope of the invention.

It is well-settled law that enablement is not precluded by the necessity for some experimentation. Moreover, enablement does not require that all encompassed embodiments be operative but rather that one skilled in the art can identify operative embodiments without engaging in undue experimentation. MPEP § 2164.06. "The test is not merely quantitative, since a considerable amount of experimentation is possible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction

in which the experimentation should proceed." (*In re Wands*, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988).

Applicants do not claim all expansins, rather Applicants claim an isolated polynucleotide encoding a protein with expansin activity detected using specific hybridization conditions, a polynucleotide having at least 90% identity with a polynucleotide of the sequence shown in SEQ ID NO: 1 or a polynucleotide identified using SEQ ID NO:1 or 7 with expansin activity, as set forth in the Published Specification, at paragraphs 142-143. Applicants submit that given the sequence SEQ ID NOS:1 and 7 along with the claims and the teaching in the specification, one of skill in the art would know how to design primers and probes and determine the PCR amplification and hybridization conditions necessary to detect a polynucleotide that is at least 90% identical to the sequence of SEQ ID NO:1 or a polynucleotide that encodes a polypeptide having at least 90% sequence identity to the sequences of SEQ ID NOS:2-7 having expansin activity.

Applicants have amended the method of claim 5 to recite "wherein a nucleotide sequence of said oligonucleotide is obtained by: aligning two or more nucleotide sequences of expansins according to sequence identity to identify a conserved sequence in said expansin sequences". Support for this amendment can be found in the Published Specification, at paragraph 196. Applicants submit that one skilled in the art can design primers and probes based on highly conserved regions among aligned nucleic acid or amino acid expansin sequences including SEQ ID NOS:1-7. Thus, it is possible to design primers that amplify other expansins and probes that detect other expansins based on knowledge from known nucleic acid or amino acid expansin sequences.

The Specification describes in detail parameters for hybridization and preparation of probes as well as parameters for PCR amplification and primers in addition to the teaching in the claims. Published Specification, paragraphs 114-116, 195-196, and 98-108. In addition, the technology for determining the hybridization of probes and PCR amplification of primers is well known in the art. See Published Specification citing Sambrook et al, at paragraphs 98, 104-05, and 195.

Applicants note that the Office Action has provided neither evidence nor sound scientific reasoning for the alleged undue experimentation required to perform the methods of the claims. Evidence that a polynucleotide that is at least 90% identical to the sequence of SEQ ID NO:1 or a polynucleotide that encodes a polypeptide having at least 90% sequence identity to the sequences of SEQ ID NOS:2-7 can be obtained using PCR or hybridization techniques can be found in more recent teachings including the Applicants' own work as well as in others skilled in the art. Published Specification, at paragraphs 114-116, 195-196, and 98-108. In support of this, Applicants direct the Examiner's attention to the Published Specification, at paragraph 196, which describes the use of degenerate primers based on the N-terminal amino acid sequence from the cucumber S2 expansin to detect S2 expansin cDNA. Importantly, the S2 expansin cDNA was successfully amplified using at least one primer based on the alignment of conserved nucleotide sequence of cucumber S1 expansin with other Arabidopsis and rice expansin cDNA sequences. In addition, Applicants respectfully direct the Examiner's attention to the literature cited in the 112 rejection, specifically U.S. Patent No. 6,350,935 issued to Bennet. In particular, Example 1 in the '935 patent describes the identification and isolation of a tomato expansin by aligning deduced amino acid sequences of the nine expansins from the Shcherban (1995) article, identifying two conserved amino acid domains from the alignment, and designing degenerate

PCR primers based on conserved regions and successfully amplifying expansin cDNA from tomato. The '935 patent and the teachings of the present invention show that one can successfully design primers based on alignments of nucleotide or amino acid sequences of known or predicted expansins such as SEQ ID NOS: 1-7 and successfully identify expansins more varied than the claimed polynucleotides having 90% or greater nucleotide or amino acid identity with SEQ ID NOS:1 and 7 using routine methods. Thus, one skilled in the art can certainly use these techniques to identify expansins having 90% or greater nucleotide identity with SEQ ID NO:1. This is in direct contrast to the Examiner's statement that it is not routine in the art to test for multiple substitutions or multiple modifications, as encompassed by instant claims 2 and 3 reciting 90% sequence identity, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity /utility.

The present application also provides standard techniques for the identification of sequences having substantial sequence similarity to the sequences of the invention, including hybridization as disclosed in Sambrook, et al., (1989) MOLECULAR CLONING: A LABORATORY MANUAL (2d ed., Cold Spring Harbor Laboratory Press, Planview, N.Y.). Published Specification, at paragraphs 98, 104-05, and 195. Furthermore, the specification at paragraphs 98-108 describes specific hybridization and washing conditions that can be employed to identify expansin polynucleotide variants that hybridize under appropriate hybridization conditions. In light of the above, Applicants submit that it would be strictly routine for one of skill in the art to detect polynucleotides having 90% identity to the sequences provided in the specification and that the work would not constitute "undue experimentation".

As shown, the Specification and '935 patent demonstrate that the methods of the invention are enabled for obtaining expansins having 90% or greater nucleotide or amino acid identity to SEQ ID NOS: 1 and 7 and expansin activity. After identifying conserved regions of expansin proteins, Applicants submit that provided with the nucleotide and amino acid sequence of SEQ ID NOS:1-7, the teachings in paragraphs 111-112 and Table 1 which provides examples of conserved amino acid substitutions, one of ordinary skill in the art would be able to make polynucleotides or polypeptides having 90% or greater nucleotide or amino acid identity to SEQ ID NOS: 1 and 7. Applicants' specification provides ample guidance to the skilled artisan seeking to confirm whether an expansin with 90% or greater sequence identity to the sequences of SEQ ID NOS:2-7 has the biological activity of an expansin protein having the amino acid sequences of SEQ ID NOS 2-7.

One of skill in the art would be able to make and use the present invention without undue experimentation using well-known techniques available prior to the priority filing date of the present application. For example, polynucleotides can be isolated or amplified from cDNA libraries or produced by using recombinant DNA technology. Published Specification, paragraphs 95, 97, and 109. Furthermore, variants of expansins can be isolated from libraries or created using standard techniques known to those skilled in the art, for example, site-directed mutagenesis, to make expansins that vary with respect to both nucleic acid and amino acid sequences. Percent identity can be calculated using computer programs known to one of skill in the art, including BLAST and other programs.

Standard techniques known to one skilled in the art can be employed to identify expansin proteins including the use of antibodies, such as those described in the Published Specification at paragraph 174. Assays to test for expansin activity are described at paragraphs 142 and 143 in

the Published Specification. These assays and techniques are routine and one of skill in the art would be able to ascertain if the polypeptide displayed expansin activity as that disclosed in the Published Specification at paragraphs 144-150. Therefore, one of skill in the art would be able to use the polynucleotides of the claimed invention without "undue experimentation".

Thus, those following the general and precise teachings of the specification can achieve identification and isolation of expansins having 90% or greater nucleotide or amino acid identity to SEQ ID NOS:1 and 7. In combination with the level of one of ordinary skill in the art and in the absence of any evidence or reasoning of record that would support a finding that the disclosure is non enabling for the claims as presently written, it is submitted that a *prima facie* of non-enablement has not been established. Applicants' invention of expansins and methods of identifying expansions is a pioneering invention. Applicants have identified a number of expansins from a wide variety of sources, including cucumber, rice, oat, *Arabidopsis*, and snail, that have expansin activity. Published Specification, at paragraph 7. As innovators in the field and based on Applicants' enabling description, Applicants respectfully submit that they are entitled to broad claim scope. For the reasons argued above, Applicants respectfully request that the Examiner withdraw the rejection.

IV. 35 U.S.C. § 112

A. Claims 3, 8 and 12 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

Claim 3, line 2 recites "retains similar biological activity". The Examiner writes that the claim is indefinite because it is not clear what similar activities are encompassed by the phrase

biological activity. The Examiner writes that substituting "retains similar biological activity" with "retains expansin activity" will overcome this rejection.

Applicants thank the Examiner for this suggestion and accordingly have adopted the Examiner's language.

B. Claim 8 depends on claim 5, and claim 5 recites "8-30 contiguous bases derived from SEQ ID NO:1". The Examiner writes that this claim is indefinite because it is not clear what derived from means as no derivations of SEQ ID NO:1 are disclosed. The Examiner writes that substituting "derived" with "obtained" will overcome this rejection.

Applicants thank the Examiner for this suggestion and accordingly have amended claim 5 so that it now recites 8-30 contiguous bases obtained from SEQ ID NO:1. Support for 8-30 contiguous bases can be found in the published specification at paragraph 7.

C. The Examiner writes that claim 12 depends on claim 11, and claim 11 recites "designing a primer based upon SEQ ID NO:7". The Examiner writes that this claim is indefinite because it is not clear how a primer which is a short, single-stranded RNA or DNA segment that functions as the starting point for polymerization of nucleotides, is obtained from a polypeptide sequence of SEQ ID NO:7, unless translated.

Applicants have amended claim 11 so that it now recites "designing a degenerate primer". Support for this amendment can be found in the Published Specification, at paragraph 196. One skilled in the art would understand the meaning of this term as used in the claim. The term "degenerate primer" as now recited in amended claim 11 is, as of Applicants' priority date, a recognized term of art referring to a primer whose design is based on an amino acid sequence. In the event that the Examiner maintains the rejection, Applicants would welcome discussions with the Examiner regarding alternative acceptable terms that are synonymous with this term that is

equally defined by the disclosure. Applicants respectfully request that these rejections be withdrawn and reconsidered.

V. 35 U.S.C. § 101

Claims 3-4, 8 and 12 stand rejected under 35 U.S.C. § 101 because the claimed invention is directed toward non-statutory subject matter. The Examiner writes that this rejection may be overcome by amending the claims 3-4, 8 and 12 to recite wording such as "an isolated polynucleotide or DNA or nucleic acid sequence".

Accordingly, claims 3-4, 8 and 12 have been amended to require "An isolated" polynucleotide or nucleotide sequence. Therefore, Applicants respectfully request that this rejection be withdrawn and reconsidered.

VI. DOUBLE PATENTING

Claims 1-4, 8 and 12 stand rejected under the judicially created doctrine of double patenting over claims 1-3 of U.S. Patent No. 6,255,466 since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

Applicants will provide a terminal disclaimer upon notification of the allowance of the pending claims.

VII. CONCLUSION

Please consider this a one-month extension of time from May 23, 2006 to June 23, 2006 and charge Deposit Account No. 26-0084 the amount of $60.00.

Please also charge Deposit Account No. 26-0084 the amount of $550.00 for 2 additional claims over 20 ($25 each) and 5 new independent claims over 3 ($100 each). No other fees or extensions of time are believed to be due in connection with this amendment; however, consider this a request for any extension inadvertently omitted, and charge any additional fees to Deposit Account No. 26-0084.

Reconsideration and allowance is respectfully requested.

Respectfully submitted,

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